REMARKS

Claims 1, 2, 15, 16 and 18-24 are pending in the subject application. By this Amendment, applicants have canceled claims 23 and 24 without prejudice or disclaimer. In view of the arguments below, applicants maintain that the Examiner's rejections have been overcome, and respectfully request that they be withdrawn.

Provisional Obviousness-Type Double Patenting Rejection

The Examiner provisionally rejected claims 1, 15, 16, and 18-24 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 27, 39, and 40 of copending U.S. Application No. 10/712,642.

Applicants understand that this provisional rejection will become non-provisional once the claims of the subject application are deemed allowable, at which time applicants will respond.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 23 and 24 under 35 U.S.C. §112, first paragraph, because the specification allegedly does not reasonably provide enablement for in vivo methods.

Without conceding the correctness of the Examiner's rejection, applicants note that claims 23 and 24 have been canceled in order to expedite prosecution of the subject application, thereby rendering the Examiner's rejection moot.

Rejection Under 35 U.S.C. §103(a)

The Examiner rejected claims 1, 2, 15, 16 and 18-22 under 35 U.S.C. §103(a) as allegedly unpatentable over Reeves et al. and Milner et al., in view of Tanigushi et al. and Au-Young et al.

In response to the Examiner's rejection, applicants respectfully traverse, and maintain that the Examiner has failed to establish a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three criteria with respect to each claim. First, the cited references, when combined, teach or suggest every element of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

In light of these requirements, applicants maintain that the cited references fail to support a *prima facie* case of obviousness for independent claims 1 and 15 and dependent claims 2, 16 and 18-24.

The rejected claims provide antisense oligonucleotides which specifically hybridize to nucleic acids encoding human DNA-PK Ku70 subunits and methods for increasing the susceptibility of a cell to DNA-damaging agents. The method of claim 1 and the antisense oligonucleotide of claim 15 are, at least in part, based on applicants' surprising discovery of Ku70's role in DNA double-stranded breaks repair.

The Examiner stated in the December 23, 2004 Final Office Action, that Reeves et al. is relied upon for teaching the nucleic acid sequence encoding the DNA-PK Ku70 subunit, and Milner et al. teaches methods of designing and testing antisense oligonucleotides. The Examiner also stated in the December 23, 2004 Final Office Action, that Tanigushi et al. teach antisense oligonucleotides which hybridize to mouse DNA-PK subunits, and Au Young et al. teach pharmaceutical compositions comprising antisense oligonucleotides. In the August 15, 2005 Office Action, the Examiner states that it would have been obvious to one of skill in the art to design and utilize antisense oligonucleotides to inhibit the expression of Ku70 in vitro because its nucleotide sequence is taught by Reeves et al., and Milner et al. teach the ability to design and assess antisense oligonucleotides for their ability to inhibit the expression of a target gene of known nucleotide sequences. The Examiner further states that one of skill in the art would have been motivated to target and inhibit the expression of Ku70 in order to increase a cell's sensitivity to DNA damaging agents because Tanigushi et al. teach the relationship between increasing cell

radiosensitivity or loss of DNA repair function.

In response to the rejection of claims 1 and 2, applicants maintain that none of the references teach a *method* for increasing the susceptibility of a cell to DNA-damaging agents, comprising introducing into the cell *in vitro* an antisense oligonucleotide that specifically hybridizes to a nucleic acid encoding a human DNA-dependent protein kinase subunit so as to prevent expression of the human DNA-dependent protein kinase subunit. None of the cited references teaches the introduction of any antisense oligonucleotide into any cell for the purpose of increasing the susceptibility of the cell to DNA-damaging agents. In addition, Takiguchi et al. does not teach *human* Ku70 but teaches *mouse* Ku70. On page 132, last paragraph, Takiguchi et al. state that the *relationship between mouse and human DNA-PKcs has not yet been established.* Takiguchi et al. further point out that the mouse and human DNA-PKcs genes have been mapped to different chromosomes *suggesting that the roles of these proteins may also be different.* In addition, applicants disagree with the Examiner's assertion that one of skill in the art would be motivated to practice such methods because the role of Ku70 in DNA repair was known in the art. On page 129, abstract, Takiguchi et al. state that the role of Ku70 in DNA double-stranded repair and V(D)J recombination has not yet been determined. Applicants maintain that absent applicants' discovery of the role of Ku70, one skilled in the art would not have been motivated to combine the cited references and practice the instant invention. Therefore, applicants maintain that the cited references in combination fail to teach each and every

element of claims 1 and 2, and provide no motivation to combine the teaching of the cited references as some elements of the claims were not yet known in the art.

In response to the rejection of claims 15, 16 and 18-22, applicants maintain that none of the cited references teaches an antisense oligonucleotide that specifically hybridizes to a nucleic acid encoding a human Ku70 subunit of DNA-PK, as provided in claim 15 and as recited in dependent claims 16 and 18-24. Takiguchi et al. teach an antisense molecule that hybridizes to *mouse* DNA-PK. Takiguchi et al. does not disclose antisense oligonucleotides hybridizing to *human* DNA-PK. Therefore, applicants maintain that the cited references in combination fail to teach each and every element of claims 15, 16 and 18-24. As stated above, applicants again maintain that there was no motivation to combine the cited references since the role of Ku70 was discovered by applicants, and was not known in the art.

In response to the rejection of claims 23 and 24, applicants note that claims 23 and 24 have been canceled in order to expedite prosecution of the subject application, thereby rendering the Examiner's rejection of these claims moot.

For the reasons above, the cited references combined fail to teach the elements of the claimed methods or the claimed antisense oligonucleotide. Absent applicants' discovery of the role of human Ku70 in DNA repair, there would have been no motivation to combine the cited references and no expectation of

success in doing so.

In view of the above remarks, applicants maintain that the Examiner has failed to set forth a *prima facie* case of obviousness, and that accordingly, claims 1, 2, 15, 16 and 18-22 satisfy the requirements of 35 U.S.C. §103(a).

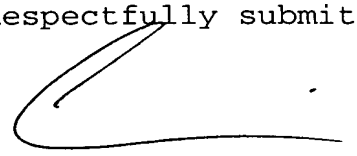
Conclusion

For the reasons set forth above, applicants respectfully request that the Examiner reconsider and withdraw the rejections, and solicit allowance of pending claims 1, 2, 15, 16 and 18-22.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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